HBB FULL GENE SEQUENCING

Specimen Description:
Sample quality is optimum for the test. DNA Conc.: 53.8 ng/ul.

Sickle cell - Beta Thalassemia Disease

Sample	HBB Variant (NM_000518.5)	Zygosity	Inheritance	Classification
Yogita Nagtilak	HBB:c.20A>T/Hb S (Exon 1) HBB:c.92+5G>C/IVS-I-5 (G>C) (Intron 1)	Likely Compound Heterozygous	AR	Pathogenic (Affected)

Variant classification as per ACMG guidelines:	
Variant	A change in a gene. This could be disease causing (pathogenic) or not disease causing (benign).
Benign	A variant which is known not to be responsible for disease has been detected. Generally, no further action is warranted on such variants when detected.
Likely Benign	A variant which is known not to be responsible for disease has been detected. Generally, no further action is warranted on such variants when detected.
Pathogenic	A disease-causing variation in a gene which can explain the patient's symptoms has been detected. This usually means that a suspected disorder for which testing had been requested has been confirmed.
Likely Pathogenic	A variant which is very likely to contribute to the development of disease however, the scientific evidence is currently insufficient to prove this conclusively. Additional evidence is expected to confirm this assertion of pathogenicity.
Variant of Uncertain	A variant has been detected, but it is difficult to classify it as either pathogenic (disease causing) or benign (non-disease causing) based on current available scientific evidence.

Significance	Further testing of the patient or family members as recommended by your clinician may be needed. It is probable that their significance can be assessed only with time, subject to availability of scientific evidence.

Recommendations:

- Genetic counselling

Background:

- HBB gene encodes beta chain of hemoglobin protein found in Red blood cells.
- Mutation in this gene causes decreased production of this protein and leads to Beta thalassemia or Sickle cell disease.
- Beta-thalassemia is an autosomal recessive disorder, depending on the type of mutation, beta-thalassemia patients experience a wide variety of symptoms, ranging from mild anemia to severe transfusion-dependent hemolyticanemia.
- There are several mutations in thalassemia -insertion, deletion, duplication, point mutations. Among all of these the five common mutations are-IVS 1-5 G > C, IVS 1 -1 G > T, Codon 41/42 (- CTTT), Codon 8/9 and the 619 bp deletion account for over 90% of the mutations in b-thalassemia population.
- This test can be useful in the patients who have symptoms, or parental carrier testing in order to diagnose prenatal.

Test Methodology:

- The test is performed by end point PCR using gene specific primers followed by automated DNA sequencing of the amplicon using Big Dye™ Terminator Chemistry on an ABI Genetic Analyzer 3500DX platform. Sequencing data were aligned to NCBI database to analyze the mutations.
- Large deletion of the HBB gene 619bp deletion is PCR amplified to check its presence.

Disclaimer:

- Large deletions/duplication that eliminates most or all of the coding sequence will also not detected by this assay. In addition, mutations in other genes associated with HBB gene will not be identified.
- Please note that variant classification and/or interpretation may change over time if more information

available.

- For questions about this report, or for assistance in locating nearby genetic counselling services, please contact the Laboratory:
- Although all precautions are taken during DNA tests the currently available data indicate that the technical error rate for all types of DNA analysis is approximately 2%. It is important that all clinicians or persons requesting DNA diagnostic tests are aware of these data before acting upon these results.

***References*:**

1. *Wheatherall DJ, Clegg JB . The thalassemia syndromes. 4th ed. Oxford, England: Blackwell Science Ltd, 2001.*
2. *Flint J, Harding RM, Boyce AJ, Clegg JB. The population genetics of the haemoglobinopathies. Baillieres Clin Haematol 1993; 6: 215–262.*
3. *Olivieri N, Weatherall DJ . Clinical aspects of β-thalassemia. In: Steinberg MH, Forget BG, Higgs DR, Nagel RL, editors. Disorders of hemoglobin, genetics, pathophysiology, and clinical management. Cambridge, England: Cambridge University, 2001; 277–341.*

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